REMARKS

Claims 1-3, 5, 6, 8-18, 60, and 63-65 are pending. Claims 1, 2, 5, 6, 8-18, and 60 have been amended, claim 3 has been cancelled without prejudice or disclaimer, and new claims 75-80 have been added. These amendments and additions add no new matter as the claim language is fully supported by the specification and original claims. The amendment to claim 1 is supported, for example, by page 3, lines 23 and by claim 3, as filed. The amendment to claims 2, 8-18, and 60 are minor typographical edits. The amendment to claims 5 and 6 clarify that the single chain antibody binds phOx. Newly added claim 75 is supported, for example, by Example 1. Newly added claim 76 is supported, for example, by page 18, lines 11-14. Newly added claim 77 is supported, for example, by SEQ ID NO:1. Newly added claim 78 is supported, for example, by page 40, lines 14-26. Newly added claim 79 is supported, for example, by page 3, lines 15-16. Newly added claim 80 is supported for example, at page 45, lines 24-26). Upon entry of the present amendment, claims 1-3, 5, 6, 8-18, 60, 63-65, and 75-80 will pending. Reconsideration of the application in light of the foregoing amendments and the following discussion is respectfully requested.

The Rejection under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 1-3, 5-6, 8-18, 60, and 63-65 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly not enabled by the specification as filed. Applicant respectfully traverses the rejection. The Office Action acknowledges that the present specification enables a variety of embodiments, as listed in points 1 to 15, starting on page 2, last paragraph of the Office Action, including methods that include a single chain antibody that binds specifically to phOx and a diaminopentane linker coupling a probe to a ligand such as phOx. However, the Office Action alleges that the specification does not enable a method that includes any ligand, any linker, and any single chain antibody, including a single chain antibody that has at least 30% sequence identity to SEQ ID NO:1 and binds phOx. The Office Action alleges that since the specification only discloses one single chain antibody and allegedly does not specifically

indicate which residues can tolerate change, it allegedly does not enable any single chain antibody.

The present disclosure provides working examples of methods for localizing a probe that include an antibody that binds phOx. The specific single chain antibody/ligand combination functions in the method to localize the probe to the vicinity of the ligand, allowing visualization of the ligand. Accordingly, a skilled artisan will recognize that virtually any antibody/ligand pair combination, of which many are known, can be successfully employed in methods of the pending claims to localize the probe to the vicinity of the ligand, provided that a conjugate that includes the ligand is membrane permeant. In fact, any specific binding partner can be used, as recited in claim 60.

Antibody molecules, including single chain antibodies, are some of the most well-characterized molecules in biotechnology. Methods are well known in the art for generating single chain antibodies against virtually any ligand, as discussed in the specification (Page 18, lines 4-19). Therefore, a skilled artisan could readily develop a single chain antibody against virtually any ligand using standard techniques. Furthermore, regarding claim 60, which recites that the method includes specific binding partners (SBPs), many SBPs are known in the art (See pages 18- 22 of the present specification). Finally, regarding claim 5, which includes a single chain antibody that has at least 30% sequence identity to SEQ ID NO:1, since antibody molecules have been well characterized, regions that are important for epitope binding, for example, can be identified from the sequence information. Therefore, a skilled artisan based on the disclosure of SEQ ID NO:1 can design variants of this sequence that will also bind phOx, for example. Accordingly, Applicant respectfully requests withdrawal of the rejection of claims 1-3, 5-6, 8-18, 60, and 63-65 under 35 U.S.C. § 112, first paragraph as allegedly not enabled by the specification as filed.

The Rejection under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 1-3, 5-6, 8-18, 60, and 63-65 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly not adequately described by the specification. Applicant respectfully

traverses the rejection. The Office Action alleges that the specification does not adequately describe a method that includes any ligand, any linker, and any single chain antibody or homolog thereof, including a single chain antibody that has at least 30% sequence identity to SEQ ID NO:1 and is capable of recognizing phOx. The Office Action alleges that because the specification discloses only one single chain antibody, SEQ ID NO:1, it does not sufficiently describe methods that include any single chain antibody (citing University of California v. Eli Lilly and Co., 43 USPQ 2d, 1398 (referred to herein as "*Regents v. Lilly*")).

Applicant respectfully asserts that the present invention is readily distinguishable over the facts of *Regents v. Lilly*. Unlike the patent claims at issue in *Regents v. Lilly*, which were directed at compositions such as recombinant microorganisms and recombinant plasmids that include an insulin-encoding cDNA, the pending claims are directed at methods of use that include a single chain antibody. The fact that the pending claims are directed at methods instead of compositions is an important distinction between the pending claims and the patent claims at issue in *Regents v. Lilly*. The present disclosure provides working examples of methods for localizing a probe that include a single chain antibody that binds phOx. The specific single chain antibody/ligand combination functions in the method to localize the probe to the vicinity of the ligand, allowing visualization of the ligand. Accordingly, a skilled artisan will recognize that virtually any antibody/ligand pair combination, of which many are known, can be successfully employed in methods of the pending claims to localize the probe to the vicinity of the ligand, provided that a conjugate that includes the ligand can be membrane permeant. A skilled artisan will recognize that single-chain antibodies are well characterized and can be generated against virtually any ligand using routine methods known in the art (See e.g., page 18, lines 4-19 of the present specification).

Another important distinction between the pending claims and those at issue in *Regents v. Lilly* is that unlike the *human* and *mammalian* insulin-encoding nucleic acids recited in the pending claims at issue in *Regents v. Lilly*, single chain antibodies recited in the methods claims of the present application are not limited to those isolated from certain species. Therefore, unlike human or mammalian insulin-encoding DNA, whose structures are defined

by nature and were unknown as of the filing date of the patents at issue in *Regents v. Lilly*, the pending claims do not recite single chain antibodies from a certain species or genera of organisms. As indicated above, any single chain antibody can be used with the present invention. The particular specificity or binding properties of the single chain antibody are not critical to the invention, except that the antibody must bind the ligand used on the conjugate. As indicated above, methods are known in the art for producing a single chain antibody against any antigenic ligand.

Claims 5-6 are further distinguishable over the claims at issue in *Regents*. These claims provide further structural definition for the single chain antibody used in the claimed methods, in that the single chain antibodies are at least 30% identical to SEQ ID NO:1, or are a homologue of SEQ ID NO:1. Single chain antibodies with homology or substantial identity to SEQ ID NO:1, are not a genus of unknown structures defined by nature, as was the case for mammalian insulin-encoding DNA at issue in the *Regents* case. Rather, one of ordinary skill can readily determine whether a sequence has sufficient sequence identity to meet the claimed limitation and retains the ability to bind phOx using standard techniques. In summary, Applicant respectfully requests withdrawal of the rejection of claims 1-3, 5-6, 8-18, 60, and 63-65 under 35 U.S.C. § 112, first paragraph as allegedly not adequately described by the specification as filed.

The Rejection under 35 U.S.C. § 103

The applicant respectfully traverses the rejection of claims 1-3, 5, 6, 8, 11-14, 16-17, 60, and 63-65 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pat. No. 6,017,754 (referred to herein as "the '754 patent") in view of Haugland et al. (Handbook of Fluorescent Probes and Research Chemicals 6th edition, pages 13-15, 18-19 (1996)) and WO 93/11120.

The Office Action alleges that the '754 patent teaches a method of identifying and selecting a cell to study genes of interest at a cellular level by transfecting the cell with a plasmid that encodes a single chain antibody (sFv) directed against phOx (citing Fig 1 A-2, Fig 6, column 1, line 54 bridging column 2 line 1, column 6, line 11 of the '754 patent). The single

chain antibody allegedly is related to the single chain antibody of SEQ ID NO: 1 of the present application. The Office Action further asserts that the '754 patent teaches that the hapten (phOx) as the ligand can be conjugated to a fluorescent (FITC) spectroscopic probe or other label via a linker moiety (phOx-BSA-FITC) to allow for identification and selection of the transfected cell by detecting fluorescence emission (citing column 7, line 8-13 of the '754 patent).

The Office Action concedes that the '754 patent does not disclose several elements of the pending claims. The Office Action acknowledges that the '754 patent does not disclose a method for localizing a probe that includes contacting a sample with a membrane permeant probe/ligand conjugate that includes a probe, a ligand, and a linker. Furthermore, regarding claims 64 and 65, the Office Action acknowledges that the '754 patent do not disclose a method wherein the probe provides a more intense signal when the probe/ligand conjugate is bound to the single chain antibody than when it is unbound.

The Office Action asserts that Haugland et al. teach spectroscopic probes that are membrane permeant, including BODIPY FL. Furthermore, the Office Action asserts that Haugland et al. teach a method of linking the BODIPY FL dye to various biomolecules for making conjugates. Regarding WO 93/11120, the Office Action alleges that this reference teaches a flexible aliphatic linker that is membrane permeant. Based on these assertions, the Office Action concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the membrane impermeant linker/probe conjugate such as BSA-FITC with BIODIPY FL taught by Haugland et al. and a linker taught by Haugland et al. or by WO 93/111020.

To establish a *prima facie* case of obviousness there must be some suggestion or motivation in the prior art to make the claimed invention, there must be a reasonable expectation of success, and the prior art reference must teach or suggest all of the claim limitations. MPEP 2142; In re Vaeck, 947 F.2d 488, 20 USPQ2d, 1438 (Fed. Cir. 1991). The mere fact that references can be combined or modified does not render the resultant combination obvious, unless the prior art also suggests the desirability of the combination.

MPEP 2143.01 citing In re Mills, 916 F.2d 680 (Fed. Cir. 1990). If the proposed modification of one prior art reference would render it unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. MPEP2143.01 citing In re Gordan, 733 F.2d 900, 221 (Fed. Cir. 1984).

The combination of the '754 patent and the cited secondary references, does not result in a method for localizing a probe within a cell, that includes a membrane permeant conjugate for detecting a single chain antibody or a specific binding pair member expressed from a recombinant nucleic acid, as recited in the pending claims. First, unlike the present invention which is directed to methods for localizing a probe within a cell, the '754 patent focuses on methods for isolating cells. This distinction is important because a skilled artisan would not be motivated to combine the '754 patent with the secondary references that allegedly provide membrane permeant probes and linkers, because there is no reason to use a membrane permeant probe to isolate cells using the methods of the '754 patent.

In fact, modifying the method taught by the '754 patent to include a membrane permeant conjugate, would render the method unfit for its recited purpose. The methods of the '754 patent involve isolation of a cell that expresses a single chain antibody on the cell's outer surface, by contacting the cell with a hapten or epitope bound to a cell separation means (Col. 6, lines 13-15). The use of a membrane permeant conjugate with the methods of the '754 patent would render such methods unfit for their intended purpose because such conjugates could not be used for cell isolation according to the methods described in the '754 patent, which utilize binding of phOx to the outer plasma membrane surface. In fact, the '754 patent teaches away from using a membrane permeant conjugate to detect an expressed single chain antibody by indicating that the single chain antibody is expressed on the surface to act as a "molecular hook" to allow isolation of a transfected cells using a cell separation means (Col. 6, lines 13-15). There is no advantage, and in fact, there would probably be undesirable effects, of using a conjugate that is membrane permeant with the methods of the '754 patent.

Furthermore, Applicant respectfully asserts that a skilled artisan would not be motivated to replace the BSA moiety of the phOx-BSA-FITC conjugates of the '754 patent,

with a linker of Haugland et al. or WO 93/11120 to attempt to make the conjugate membrane permeant. In hindsight, the Office Action characterizes BSA as a "linker" in the conjugates of the '754 patent. However, a skilled artisan would conclude that BSA serves more than a linker function in the conjugates taught by the '754 patent. If the '754 patent desired only to directly link phOx and FITC moieties, they would not have selected a large protein such as BSA as a linker. Rather, a skilled artisan would conclude that BSA in the phOx-BSA-FITC conjugates serves a purpose in addition to, or other than, linking the FITC moiety and phOx. Therefore, a skilled artisan would not be motivated to use a small membrane permeable linker, as allegedly taught by Haugland et al. and WO 93/11120, in place of BSA in the conjugates of the '754 patent.

Even if a linker of Haugland et al. and the '754 patent is substituted for BSA in the conjugates of the '754 patent, the conjugate would still not be membrane permeant. the '754 patent describes transfecting cells with a nucleic acid capable of expressing a single chain antibody that recognizes a ligand, and isolating transfected cells using a "cell separation means" coupled to a ligand. (Col. 7, lines 3-10 ("this hapten or epitope is bound either directly or indirectly to a cell separation means.... The hapten or epitope *can also include* or be conjugated to a fluorescent or other labeled, selectable hapten or epitope ." (emphasis added))). The cell separation means renders the conjugate membrane permeant regardless of the moiety chosen to link PhOX with FITC.

Specifically with respect to WO 93/11120, Applicant respectfully asserts that one of ordinary skill in the art would not be motivated or have a reasonable expectation of success in using the linker disclosed in WO 93/11120 in conjugates of the '754 patent or conjugates of the present invention. This conclusion is based on the fact that the linker disclosed in WO 93/11120 is for linking conjugates in which one of the conjugated molecules is a lipophilicyanin precursor molecule (See WO 93/11120, page 25, line 15). In conjugates of the '754 patent, or the present invention, the ligand is not a lipophilicyanin precursor molecule. Accordingly, Applicant respectfully asserts that one of ordinary skill in the art would not be

motivated or have a reasonable expectation of success in using the linker disclosed in WO 93/11120 in conjugates of the '754 patent or conjugates of the present invention.

Regarding claims 64 and 65, directed to methods whereby the probe provides a more intense signal when the probe/ligand conjugate is bound than unbound, the Office Action alleges that these claims are rendered obvious by the cited art because the intensity of the signal is allegedly an inherent property of the probe. Applicant respectfully asserts that this is not an inherent property of the probe, but rather is a result of the stacking of unbound probe by the ligand within the conjugate as a result of a flexible linker (Page 42, lines 9-11). The cited art is silent as to conjugates with this characteristic. This is significant because a reduced signal of unbound probe improves the performance of the method (See page 43, lines 13-16). In summary, Applicant respectfully requests withdrawal of the rejection of claims 1-3, 5, 6, 8, 11-14, 16-17, 60, and 63-65 under 35 U.S.C. § 103(a) as allegedly unpatentable over the '754 patent in view of Haugland et al. and WO 93/11120.

The Office Action rejects claim 9 under 35 U.S.C. 103(a) as being unpatentable over the '754 patent (US Pat No. 6,017,754) in view of Haugland et al. (Handbook of Fluorescent Probes and Research Chemicals 6th edition, 1996, pages 13-15, 18-19) and WO 93/11120, as applied to claims 1-3, 5, 6, 8, 11-14, 16-17, 60 and 63-65, as discussed above, and further in view of Lauffer et al (U.S. Pat No. 5,628,982). Applicant respectfully traverses the rejection. The Office Action asserts that the claimed invention of claim 9 differs from the '754 patent, Haugland et al., and WO 93/11120 only by the recitation that detecting is by means of NMR imaging. The Office Action asserts that Lauffer et al. teaches hydroxyl-aryl metal chelates as NMR contrast agents or probes for diagnostic NMR imaging, and alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute hydroxy-aryl metal chelates as NMR contrast agents taught by the Lauffer et al., with the BIODIPY FL probe taught by Haugland or the fluorescein (FITC) probe conjugated to the phOx ligand as taught by the '754 patent for NMR imaging. Furthermore, the Office Action alleges that one would have been motivated, with a reasonable expectation of success, to

substitute hydroxy-aryl metal chelates as NMR contrast agents taught by Lauffer et al., for NMR imaging because the gadolinium ion with seven unpaired electrons can be used with any chelating agent having a number of open sites, it can act as a contrast agent at very low dosages, and is no more toxic than iron when used with a chelating agent having no open sites as taught by Lauffer et al.

Applicant respectfully asserts that Lauffer et al. does not overcome the deficiencies of the '754 patent, Haugland et al., or WO 93/11120 either when taken individually or in combination. As discussed above, the combination of the '754 patent, Haugland et al., or WO 93/11120, does not result in a method for detecting a label within a cell that utilizes a membrane permeant conjugate for detecting a single chain antibody or a specific binding pair member expressed from a recombinant nucleic acid. The use of the NMR enhancing agents of Lauffer et al., with the conjugates of the '754 patent would not change the fact that such conjugates are not membrane permeant. As discussed above, this impermeable property is the result of the presence and size of the second ligand and the cell separation means and not the probe. Furthermore, Lauffer et al. does not suggest modifying the method of the '754 patent to localize a probe within a cell.

Furthermore, there is no suggestion or motivation to combine Lauffer et al. with the '754 patent. As discussed above, the '754 patent is directed at methods of isolating cells using cell separating means. Lauffer et al. does not involve and is not related to cell isolation or separation. Therefore, one of ordinary skill in the art would not be motivated to combine Lauffer et al. with the '754 patent. Furthermore, one would not be motivated to make this combination because Lauffer et al. does not teach a method that includes single chain antibodies that bind the small organic ligands disclosed in Lauffer et al. Therefore, Applicant respectfully requests withdrawal of the rejection of claim 9 under 35 U.S.C. § 103 as obvious over the '754 patent in view of Haugland et al., WO 93/11120 and Lauffer et al.

The Office Action rejects claim 10 under 35 U.S.C. § 103(a) as being unpatentable over the '754 patent (US Pat No. 6,017,754) in view of Haugland et al. and WO 93/11120 as applied

to claims 1-3, 5, 6, 8, 11-14, 16-17, 60, and 63-65, and further in view of Green et al (U. S. Pat No. 5,324,502). Applicant respectfully traverses the rejection. The Office Action asserts that the claimed invention of claim 10 differs from the '754 patent, Haugland et al., and WO 93/11120 only by the recitation of detecting by positron emission tomography PET. The Office Action asserts that Green et al. teaches radiopharmaceuticals for PET wherein the radiopharmaceutical is a positron emitting gallium-68(III) cationic complex or lipophilic complex which is membrane permeant due to its lipophilic content. The Office Action alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the positron emitting gallium-68(1II) cationic complex or lipophilic complex taught by the Green et al. patent with the BIODIPY FL probe taught by Haugland et al. or the fluorescein (FITC) probe conjugated to the phOx ligand as taught by the '754 patent for PET as taught by Green et al.

Applicant respectfully asserts that Green et al. does not overcome the deficiencies of the '754 patent, Haugland et al., or WO 93/11120. As described above, the combination of the '754 patent, Haugland et al., or WO 93/11120 does not result in a method which utilizes a membrane permeant conjugate for detecting a single chain antibody or a specific binding pair member expressed from a recombinant nucleic acid. The use of the radiopharmaceuticals for PET of Green et al., in the conjugates of the '754 patent, would not change the fact that such conjugates are not membrane permeant. As discussed above, this impermeable property is the result of the presence and size of the second ligand and the cell separation means and not the probe.

Furthermore, there is no suggestion or motivation to combine Green et al. with the '754 patent, Haugland et al., or WO 93/11120. As discussed above, the '754 patent is directed at methods of isolating cells using a cell separating means. Green et al. does not involve and is not related to cell isolation or separation. Therefore, one of ordinary skill in the art would not be motivated to combine Green et al. with the '754 patent. Furthermore, one would not be motivated to make this combination because Green et al. does not teach a method that includes single chain antibodies that bind the metal chelating ligands and radioactive metals disclosed

therein. Therefore, Applicant respectfully requests withdrawal of the rejection of claim 10 under 35 U.S.C. § 103 as obvious over the '754 patent in view of Haugland et al., WO 93/11120 and Green et al.

The Office Action rejected claim 15 under 35 U.S.C. § 103(a) as being unpatentable over the '754 patent, Haugland et al., or WO 93/11120 as applied to claims 1-3, 5, 6, 8, 1-14, 16-17, 60, and 63-65 and further in view of Rizzuto et al (*Current Biology* 5(6): 635-642 (1995)). Applicant respectfully traverses the rejection. The Office Action asserts that the claimed inventions of these claims differs from the teachings of the '754 patent, Haugland et al., or WO 93/11120 by the steps of adding a stimulus to the cell and detecting the probe/ligand conjugate before and after adding the stimulus. The Office Action alleges that Rizzuto et al. teaches a method that includes detecting a GFP conjugate before and after adding the stimulus. Furthermore, the Office Action alleges that it would have been obvious for one of ordinary skill in the art at the time the invention was made to detect the conjugate before and after adding a stimulus to the methods of the '754 patent, Haugland et al., or WO 93/11120, according to the teachings of Rizzuto et al.

Applicant respectfully asserts that Rizzuto et al. does not overcome the deficiencies of the '754 patent, Haugland et al., or WO 93/11120, either individually or in combination. As described above, the combination of the '754 patent, Haugland et al., or WO 93/11120 does not result in a method for localizing a probe within a cell that utilizes a membrane permeant conjugate for detecting a single chain antibody or a specific binding pair member expressed from a recombinant nucleic acid. The use of GFP as taught by Rizzuto et al., in the conjugates of the '754 patent, would not change the fact that such conjugates are not membrane permeant. GFP is a relatively large, membrane impermeant probe. The conjugates of the '754 patent are rendered membrane impermeant by the BSA moiety and the cell separation means included in the conjugates. Therefore, changing the probe will not change the fact that BSA and the cell separation means render the conjugate impermeable. Accordingly, Applicant respectfully

requests withdrawal of the rejection of claim 15 under 35 U.S.C. § 103 as obvious over the '754 patent in view of Haugland et al., WO 93/11120 and Rizzuto et al.

The Office Action rejected claim 18 under 35 U.S.C. 103(a) as being unpatentable over the '754 patent, Haugland et al., or WO 93/11120 as applied to claims 1-3, 5, 6, 8, 1-14, 16-17, 60, and 63-65 and further in view of Youn et al (*Analytical Biochemistry* 232: 24-30, 1995). Applicant respectfully traverses the rejection. The Office Action asserts that the claimed inventions of these claims differs from the teachings of the '754 patent, Haugland et al., or WO 93/11120 by measuring fluorescence anisotropy of the probe. The Office Action indicates that Youn et al. teaches the use of fluorescence energy transfer immunoassay (FRET) based on the use of a ruthenium metal ligand complex, and that it would have been obvious for one of ordinary skill in the art at the time the invention was made to substitute the ruthenium metal ligand complex probe taught by Youn et al. for the BIODIPY FL probe taught by Haugland et al. or the fluorescein (FITC) probe taught by the '754 patent for a FRET assay. The Office Action alleges that one would have been motivated with a reasonable expectation of success, to substitute the ruthenium metal ligand complex taught by Youn et al. because the ruthenium complex allegedly has a long decay time, and is chemically and photochemically stable, thereby rendering it advantageous in time-resolved immunoassays.

Applicant respectfully asserts that Youn et al. does not overcome the deficiencies of the '754 patent, Haugland et al., or WO 93/11120, either individually or in combination. As described above, the combination of the '754 patent, Haugland et al., or WO 93/11120 does not result in a method for localizing a probe within a cell that utilizes a membrane permeant conjugate for detecting a single chain antibody or a specific binding pair member expressed from a recombinant nucleic acid. The teachings of Youn et al. do not overcome this deficiency. The use of the FRET immunoassays of Youn et al. with the conjugates of Chesnut would not change the fact that such conjugates are not membrane permeant. As discussed above, the impermeability of the conjugate is the result of the presence and size of the second ligand

and/or the cell separation means, and not the probe. Therefore, changing the nature of the probe will not make the conjugate membrane permeant.

Furthermore, there is no suggestion or motivation to combine Youn et al. with the '754 patent, Haugland et al., or WO 93/11120. As discussed above, the '754 patent is directed at methods of isolating cells using a cell separating means. Youn et al. does not involve and is not related to cell isolation or separation. Therefore, one of ordinary skill in the art would not be motivated to combine Youn et al. with the '754 patent. Furthermore, the immunoassays of Youn et al. require a labeling of both donor and acceptor, which is not compatible with the methods of the '754 patent. The methods of the '754 patent require that a single chain antibody is expressed on the surface of a living cells. This does not appear to be compatible with the methods of Youn et al. in which an isolated antibody is labeled with the RB4 acceptor *in vitro*. Therefore, Applicant respectfully requests withdrawal of the rejection of claim 18 under 35 U.S.C. § 103 as obvious over the '754 patent in view of Haugland et al., WO 93/11120 and Youn et al.

In view of the above remarks, reconsideration and favorable action on all claims is respectfully requested. Should any questions remain in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved. Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

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